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| APPLICATION NO.   | FILING DATE   | FIRST NAMED INVENTOR | ATTORNEY DOCKET NO. | CONFIRMATION NO. |
|---|---|----------------------|---------------------|------------------|
| 10/777,405  | 02/12/2004  | Seogchan Kang        | P06605US00 .        | 5865             |
| 27407 7590 05/17/2007 MCKEE, VOORHEES & SEASE, P.L.C. ATTN: PENNSYLVANIA STATE UNIVERSITY |   |                      | EXAMINER            |                  |
|   |   |                      | VOGEL, NANCY S .    |                  |
|   | 801 GRAND AVENUE, SUITE 3200<br>DES MOINES, IA 50309-2721 |                      | ART UNIT            | PAPER NUMBER     |
| ŕ   |   |                      | 1636                |                  |
|   |   | •                    |                     |                  |
|   |   |                      | MAIL DATE           | DELIVERY MODE    |
|   |   |                      | 05/17/2007          | PAPER            |

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

|  |  | ·   |  |  |  |
|--|--|---|--|--|--|
|  | Application No.  | Applicant(s)  |  |  |  |
|  | 10/042,421   | SACKSTEIN, ROBERT   |  |  |  |
| Office Action Summary  | Examiner   | Art Unit  |  |  |  |
| T. 1111110001TE 1111   | Phillip Gambel   | 1644  |  |  |  |
| The MAILING DATE of this communication app<br>Period for Reply   | ears on the cover sheet with   | the correspondence address  |  |  |  |
| A SHORTENED STATUTORY PERIOD FOR REPLY THE MAILING DATE OF THIS COMMUNICATION.  - Extensions of time may be available under the provisions of 37 CFR 1.1: after SIX (6) MONTHS from the mailing date of this communication.  - If the period for reply specified above is less than thirty (30) days, a reply - If NO period for reply is specified above, the maximum statutory period v - Failure to reply within the set or extended period for reply will, by statute Any reply received by the Office later than three months after the mailing earned patent term adjustment. See 37 CFR 1.704(b). | 36(a). In no event, however, may a rep<br>y within the statutory minimum of thirty (<br>vill apply and will expire SIX (6) MONTH<br>, cause the application to become ABAI | ly be timely filed  30) days will be considered timely.  45 from the mailing date of this communication.  NDONED (35 U.S.C. § 133). |  |  |  |
| Status   |  |   |  |  |  |
| 1) Responsive to communication(s) filed on 22 Ja   | anuary 2004.   |   |  |  |  |
| 2a) This action is <b>FINAL</b> . 2b) This action is non-final.  |  |   |  |  |  |
| 3) Since this application is in condition for allowance except for formal matters, prosecution as to the merits is   |  |   |  |  |  |
| closed in accordance with the practice under Ex parte Quayle, 1935 C.D. 11, 453 O.G. 213.  |  |   |  |  |  |
| Disposition of Claims  |  |   |  |  |  |
| 4) ☐ Claim(s) 1-61 is/are pending in the application. 4a) Of the above claim(s) 8-61 is/are withdrawr 5) ☐ Claim(s) is/are allowed. 6) ☐ Claim(s) 1-7 is/are rejected. 7) ☐ Claim(s) is/are objected to. 8) ☐ Claim(s) are subject to restriction and/o  | n from consideration.  |   |  |  |  |
| Application Papers   |  |   |  |  |  |
| 9) The specification is objected to by the Examine   | r.   |   |  |  |  |
| 10) The drawing(s) filed on is/are: a) accepted or b) objected to by the Examiner.   |  |   |  |  |  |
| Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).  |  |   |  |  |  |
| Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).  11) The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.   |  |   |  |  |  |
| 11) I he oath or declaration is objected to by the Ex  | caminer. Note the attached (   | Office Action or form PTO-152.  |  |  |  |
| Priority under 35 U.S.C. § 119   |  |   |  |  |  |
| 12) Acknowledgment is made of a claim for foreign  a) All b) Some * c) None of:  1. Certified copies of the priority document:  2. Certified copies of the priority document:  3. Copies of the certified copies of the priority document:  application from the International Bureau  * See the attached detailed Office action for a list  | s have been received.<br>s have been received in Apprity documents have been re<br>u (PCT Rule 17.2(a)).   | plication No eceived in this National Stage   |  |  |  |
| Attachment(s)  |  |   |  |  |  |
| 1) Notice of References Cited (PTO-892)  |  | mmary (PTO-413)   |  |  |  |
| 2) Notice of Draftsperson's Patent Drawing Review (PTO-948) 3) Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date   | 5) Notice of Info  | Mail Date<br>ormal Patent Application (PTO-152)<br>LCE ないのマッツのでは、これも<br>シにひられて、よいにて   |  |  |  |

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## **DETAILED ACTION**

1. Applicant's election without traverse of Invention I (claims 1-7) on 1/22/04 is acknowledged.

Claims 8-61 are withdrawn from further consideration by the examiner, 37 C.F.R. § 1.142(b) as being drawn to nonelected inventions.

Claims 1-7 are under consideration in the instant application.

2. This application contains sequence disclosures that are encompassed by the definitions for nucleotide and/or amino acid sequences set forth in 37 CFR 1.821(a)(1) and (a)(2). However, this application fails to comply with the requirements of 37 CFR 1.821 through 1.825 for the reason(s) set forth on the attached Notice To Comply With Requirements For Patent Applications Containing Nucleotide Sequence And/Or Amino Acid Sequence Disclosures.

See Table 1 on pages 10-11 of the instant specification and claims 1-7.

Applicant is required to identify all sequences with the appropriate SEQ ID NOS.

Applicant is required to fulfill these requirements.

- 3. The filing date of the instant claims is deemed to be the filing date of instant application USSN 60/240,987, i.e. 10/18/2000.
- 4. The title of the invention is not descriptive. A new title is required that is clearly indicative of the invention to which the claims are directed. Applicant should restrict the title to the <u>claimed</u> invention.
- 5. The application is required to be reviewed and all spelling, TRADEMARKS, and like errors corrected.

Trademarks should be capitalized or accompanied by the ™ or ® symbol wherever they appear and be accompanied by the generic terminology. Although the use of trademarks is permissible in patent applications, the proprietary nature of the trademarks should be respected and every effort made to prevent their use in any manner which might adversely affect their validity as trademarks.

Appropriate corrections are required

The following is a quotation of the first paragraph of 35 U.S.C. § 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

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7. Claims 1-6 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. This is a written description rejection.

The specification broadly describes and the claims recite as part of the invention the following:

"A substantially purified glycosylated polypeptide, said glycosylated polypeptide comprising the amino acid sequence at least similar to SEQ ID NO: 1, and wherein said glycosylated polypeptide binds to an antibody having the binding specificity of monoclonal antibody HECA-452".

Such "95% similar to SEQ ID NO: 1 polypeptides" do not meet the written description provision of 35 USC 112, first paragraph.

<u>Vas-Cath Inc. v. Mahurkar</u>, 19 USPQ2d 1111, makes clear that "applicant must convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in possession of the invention. The invention is, for purposes of the 'written description' inquiry, whatever is now claimed." (See page 1117.) The specification does not "clearly allow persons of ordinary skill in the art to recognize that [he or she] invented what is claimed." (See <u>Vas-Cath</u> at page 1116.).

Applicant relies upon identifying the KG1a CD44 glycoprotein by SEQ ID NO:1 and certain other features. However, there is insufficient written description of additional species of KG1a CD44 glycoproteins which are 95% similar to SEQ ID NO:1. The skilled artisan cannot envision the broad genus of the claimed "95% similar to SEQ ID NO:1 glycosylated polypeptides".

In the absence of a nexus between structural and functional characteristics that are shared by members of the genus of KG1a CD44 glycoproteins, including those "95% similar to SEQ ID NO: 1", one of skill in the art would reasonably conclude that the disclosure fails to provide a representative number of species to describe the genus. Thus, Applicant was not in possession of the claimed genus. See <u>University of California v. Eli Lilly and Co. 119 F.3d 1559</u>, 43 USPQ2d 1398 (Fed. Cir. 1997).

In the absence of a detailed chemical structure of the "95% identical to SEQ ID NO: 1 glycosylated polypeptides" which are KG1a CD44 glycoproteins and therefore conception cannot be not achieved until reduction to practice has occurred, regardless of the complexity or simplicity of the method of isolation. Adequate written description requires more than a mere statement that it is part of the invention and reference to a potential method for isolating it. Here, defining structural features are required. See Fiers v. Revel, 25 USPQ2d 1601, 1606 (CAFC 1993) and Amgen Inc. V. Chugai Pharmaceutical Co. Ltd., 18 USPQ2d 1016. One cannot describe what one has not conceived. See Fiddes v. Baird, 30 USPQ2d 1481, 1483. In Fiddes v. Baird, claims directed to mammalian FGF's were found unpatentable due to lack of written description for the broad class.

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While actual reduction to practice is only one of several ways to satisfy the Written Description Requirement; The Guidelines for the Examination of Patent Applications Under the 35 U.S.C. 112, ¶ 1 "Written Description" Requirement make clear that if a claimed genus does not show actual reduction to practice for a representative number of species; then the Requirement may be alternatively met by reduction to drawings, or by disclosure of relevant, identifying characteristics, i.e., structure or other physical and or chemical properties, by functional characteristics coupled with a known or disclosed correlation between function and structure, or by a combination of such identifying characteristics, sufficient to show the applicant was in possession of the genus (Federal Register, Vol. 66, No. 4, pages 1099-1111, Friday January 5, 2001, see especially page 1106 3rd column).

Applicant is directed to the Guidelines for the Examination of Patent Applications Under the 35 U.S.C. 112, ¶ 1 "Written Description" Requirement, Federal Register, Vol. 66, No. 4, pages 1099-1111, Friday January 5, 2001.

Applicant is reminded that <u>Vas-Cath</u> makes clear that the written description provision of 35 USC 112 is severable from its enablement provision. (See page 1115.)

8. Claims 1-6 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for the KG1a CD44 glycosylated polypeptide comprising SEQ ID NO:1 and certain other features, does not reasonably provide enablement for any KG1a CD44 glycosylated polypeptides which is "95% similar to SEQ ID NO: 1".

The specification does not enable any person skilled in the art to which it pertains, or with which it is most clearly connected, to make and use the invention commensurate in scope with these claims.

Applicant has not provided sufficient biochemical information, particularly the nexus between the structure of SEQ ID NO: 1 and the genus of KG1a CD44 glycosylated polypeptides encompassed by the "95% similar to SEQ ID NO: 1".

Reasonable correlation must exist between the scope of the claims and scope of enablement set forth.

Since the amino acid sequence of a polypeptide determines its structural and functional properties, predictability of which changes can be tolerated in a polypeptide's amino acid sequence and still retain similar functionality (e.g. L-selectin ligand or E-selectin ligand) requires a knowledge of and guidance with regard to which amino acids in the polypeptide's sequence, if any, are tolerant of modification and which are conserved (i.e. expectedly intolerant to modification), and detailed knowledge of the ways in which a polypeptide's structure relates to its functional usefulness. However, the problem of predicting polypeptide structure from mere sequence data of a single amino acid sequence and in turn utilizing predicted structural determinations to ascertain binding or functional aspects KG1a L-selectin analogs and finally what changes can be tolerated with respect thereto is complex and well outside the realm of routine experimentation.

<u>In re Fisher</u>, 166 USPQ 18 indicates that the more unpredictable an area is, the more specific enablement is necessary in order to satisfy the statute.

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For example, Skolnick et al. (Trends in Biotech., 18(1):34-39, 2000) teach that the skilled artisan is well aware that assigning functional activities for any particular protein or protein family based upon sequence homology is inaccurate, in part because of the multifunctional nature of proteins (e.g., "Abstract" and "Sequence-based approaches to function prediction", page 34). Even in situations where there is some confidence of a similar overall structure between two proteins, only experimental research can confirm the artisan's best guess as to the function of the structurally related protein (see in particular "Abstract" and Box 2).

Because of the lack of sufficient guidance and predictability in determining which modifications would lead to "95% sequence similar to SEQ ID NO: 1" which would be a KG1a CD44 glycoprotein and that the relationship between the sequence of a peptide and its tertiary structure (i.e. its activity) was not well understood and was not predictable (e.g. see Ngo et al., in <a href="The Protein Folding Problem and Tertiary Structure Prediction">The Protein Folding Problem and Tertiary Structure Prediction</a>, 1994, Merz et al., (ed.), Birkhauser, Boston, MA, pp. 433 and 492-495.); it would require an undue amount of experimentation for one of skill in the art to arrive at enabling the genus of KG1a CD44 glycosylated polypeptides which are "95% similar to SEQ ID NO: 1".

Without sufficient guidance, making and using the claimed "KG1a CD44 glycosylated polypeptides" which are "95% similar to SEQ ID NO: 1" is unpredictable and the experimentation left to those skilled in the art is unnecessarily, and improperly, extensive and undue

9. Claims 1-7 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention

<u>Claims 1-7:</u> It is apparent that the HECA-452 antibody is required to practice the claimed invention. As a required element, it must be known and readily available to the public or obtainable by a repeatable method set forth in the specification. If it is not so obtainable or available, the enablement requirements of 35 USC 112, first paragraph, may be satisfied by a deposit of the cell line / hybridoma which produces this antibody. See 37 CFR 1.801-1.809.

In addition to the conditions under the Budapest Treaty, applicant is required to satisfy that all restrictions imposed by the depositor on the availability to the public of the deposited material will be irrevocably removed upon the granting of a patent in U.S. patent applications.

Amendment of the specification to recite the date of deposit and the complete name and address of the depository is required. As an additional means for completing the record, applicant may submit a copy of the contract with the depository for deposit and maintenance of each deposit.

If the original deposit is made after the effective filing date of an application for patent, the applicant should promptly submit a verified statement from a person in a position to corroborate the fact, and should state, that the biological material which is deposited is a biological material specifically identified in the application as filed, except if the person is an attorney or agent registered to practice before the Office, in which the case the statement need not be verified. See MPEP 1.804(b).

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reconstruction based upon hindsight reasoning. But so long as it takes into account only knowledge which was within the level of ordinary skill at the time the claimed invention was made, and does not include knowledge gleaned only from the applicant's disclosure, such a reconstruction is proper. See *In re McLaughlin*, 443 F.2d 1392, 170 USPQ 209 (CCPA 1971).

In response to applicant's argument that there is no suggestion to combine the references, the examiner recognizes that obviousness can only be established by combining or modifying the teachings of the prior art to produce the claimed invention where there is some teaching, suggestion, or motivation to do so found either in the references themselves or in the knowledge generally available to one of ordinary skill in the art. See *In re Fine*, 837 F.2d 1071, 5 USPQ2d 1596 (Fed. Cir. 1988)and *In re* Jones, 958 F.2d 347, 21 USPQ2d 1941 (Fed. Cir. 1992). In this case, the first reference teaches the general method of transformation and recombination, comprising using Agrobacterium comprising a vector containing a targeting construct comprising a first polynucleotide sequence encoding a negative selection marker linked to a fragment of DNA flanked by DNA sequences homologous to a polynucleotide to be targeted, wherein said DNA fragment is disrupted by a positive selection marker, and selecting transformants by subjecting a transformed host cell to a positive and a negative selection agent. The secondary references each teach that fungal cells can be be transformed using Agrobacterium tumefaciens, and further specifically mention a wide variety of filamentous fungi, including Aspergillus, Fusarium, and Neurospora species in addition to plant cells and such yeast as S. cerevisiae, and GrosjeanApplication/Control Number: 10/777,405 Page 7

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Courneyer et al. disclose transformation using Agrobacterium tumefaciens of a wide variety of fungi including Magnaporthe grisea, Aspergillus fumigatus, Botrytis cineria, and all Fusarium species (see col. 6 line 45 – col. 7 line 9). Therefore, it is considered that one of skill in the art would have been motivated to use any technique involving Agrobacterium transformation, including using recombination and selection techniques known to be facilitated by such transformation, in a fungal host cell of interest, since the prior art taught both techniques for obtaining homologous recombination and selection using markers, via Agrobacterium transformation, and the use of Agrobacterium transformation in fungal cells.

The following is a new rejection necessitated by applicant's amendment:

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 4 and 12-14 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

The claims are vague and indefinite since they are dependent on cancelled claim

3. In the interest of compact prosecution, the claims are examined as if they are dependent on claim 1.

## Conclusion

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Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Nancy T. Vogel whose telephone number is (571) 272-0780. The examiner can normally be reached on 7:00 - 3:30, Monday - Friday.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Joseph Woitach can be reached on (571) 272-0739. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

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Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

NV 5/7/07 NANCY VOGEL PRIMARY EXAMINER

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